

Complementation between specific HLA-DR and HLA-DQ genes in transgenic mice determines susceptibility to experimental autoimmune encephalomyelitis.

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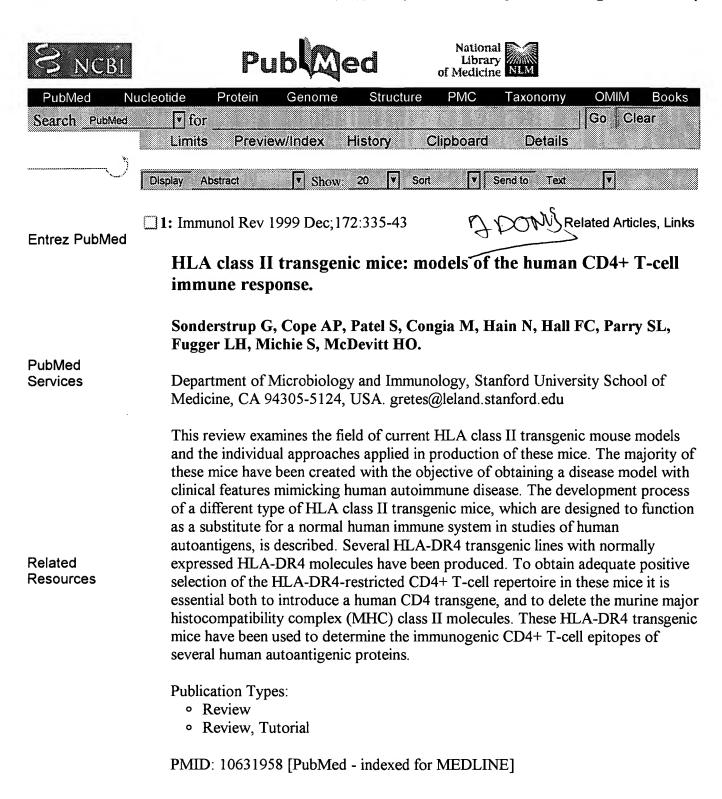
To investigate the contribution of human leukocyte antigen (HLA) class II molecules in susceptibility to inflammatory demyelination, we induced experimental autoimmune encephalomyelitis (EAE) in transgenic (tg) mice expressing the HLA-DR3, HLA-DQ8 and HLA-DQ6 molecules in the absence of endogenous class II (Ab(o)). Following immunization with mouse myelin, HLA-DR3 tg mice mounted strong T-cell proliferative responses, and developed inflammatory lesions and demyelination in the central nervous system with mild to moderate clinical symptoms of EAE. HLA-DO8 and HLA-DO6 tg mice elicited weak T-cell proliferative responses and did not develop clinical symptoms of EAE. HLA-DR3/DO6 double tg mice immunized with mouse myelin experienced clinical disease similar to the single tg HLA-DR3 tg mice, indicating that expression of DQ6 in this line had no effect on disease. In contrast, HLA-DR3/DQ8 double tg mice developed severe inflammatory lesions and clinical disease in response to immunization with mouse myelin. Our data suggest that in the presence of two susceptible class II alleles, namely HLA-DR3 and DQ8, there is additional selection and expansion of potential autoreactive T cells, resulting in enhanced severity of disease.

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